CIRUS

CENTRE FOR INTEGRATED RESEARCH AND UNDERSTANDING OF SLEEP

RESEARCH GUIDE

AUTUMN 2012

An information, recruitment and selection periodical for Physicians and Clinicians

Current Research being undertaken at The Australian Centre for Chronobiology, Endocrinology and Sleep Sciences, Woolcock Institute of Medical Research and the Brain and Mind Research Institute, University of Sydney

THE ACCESS LABORATORY

The Australian Centre for Chronobiology, Endocrinology and Sleep Sciences (ACCESS) Laboratory has been established on Level 2, Woolcock Institute of Medical Research, 431 Glebe Point Road, Glebe, NSW to facilitate translational research studies that require intensive subject/patient physiological monitoring. The centre allows close control of time awareness, light, temperature, sound and sleep. The centre can be operated in time isolation mode or with varying light intensity and varied light spectra. One room is specifically designed for controlled exposure to noise of varying type and intensity including infrasound. For example, such a facility could be used for research into health effects of wind turbine noise and traffic noise.

The centre is particularly suited to studies of simulated jet lag, shiftwork or forced desynchrony to separate the sleep and circadian systems. Novel local developed tools that are available include the AusEd computerised driving task and automated quantitative EEG analysis including detrended fluctuation analysis and power spectral analysis. New computerised modelling tools for the prediction of sleep and circadian state developed by Professor Peter Robinson's group at the University of Sydney are being implemented in the centre. The centre can also be used for non-sleep based translation studies - for example, ACCESS has also been used for carefully controlled studies of the influence of dietary protein on eating (Gosby AK, Conigrave AD, Lau NS, Iglesias MA, Hall RM, Jebb SA, Brand-Miller J, Caterson ID, Raubenheimer D, Simpson SJ. Testing protein leverage in lean humans: a randomised controlled experimental study. PLoS One. 2011;6(10):e25929)

The centre is unique in Australia for the ability to control the research environment for different types of human experimentation.

Current senior staff includes Interim Manager, Darren O'Brien PhD and Chief Technologist, Anna Mullins MSc.

The centre has 6 rooms equipped with ambulatory or fixed polysomnography monitoring equipment (funding obtained by the Woolcock Institute from the Commonwealth Government and the University of Sydney NHMRC Equipment Fund), neurocognitive testing room, patient lounge, a self contained Noise Suite and Chronobiology Suite.

Our specially trained staff are skilled in patient recruitment, polysomnography, AusEd driving simulator operation, neurocognitive testing, phlebotomy, pulsatile blood sampling and a range of other testing procedures.

Patient Information

We are constantly recruiting for any one of our existing or upcoming research protocols. We look forward to your support in advancing Australian based sleep medicine research, through conveying to your patients that they may be suitable for one or more of the studies listed in this booklet.

The ACCESS laboratory is located on Level 2, Woolcock Institute of Medical Research, 431 Glebe Point Road, on the Corner of Glebe Point Road and Leichhardt Street, Glebe. The nearest cross streets are Cotter Lane and Leichhardt Street. The ACCESS laboratory is approximately 25 minutes from Sydney Airport by road and 40 minutes walk from Central Station. Wheelchair access is available via the Ground Level lift.

Some unrestricted on-street parking is available in the neighbouring streets to the west of Glebe Point Road.

Patients using public transport will be advised that there is a bus stop located directly in front of 431 Glebe Point Road.

State Transit buses service the area and link with a number of ferry and rail services: (call 131 500 for timetables and maps, or visit www.131500.info)
431: Daily full-time service between Glebe Point, Glebe, George Street City and Millers Point.
433: Daily full-time service between Balmain and Millers Point.
370: Daily daytime service between Leichhardt and Coogee.
434: Daily early morning service between Balmain and Millers Point.
432: Daily evening service between Birchgrove.

Light Rail
The Metro Light Rail runs from Central Station to Glebe. The closest stations are 'Glebe' and 'Jubilee'. For information call (02) 9285 5600.

For further information or referrals please contact:
Inger Quinn, phone 02 9114 0007, email inger.quinn@sydney.edu.au or fax 02 9114 0465.
Darren O'Brien, phone 02 9114 0259 or email darren.obrien@sydney.edu.au or Anna Mullins, phone 02 9114 0262 or email anna.mullins@sydney.edu.au.

THE BMRI LABORATORY

The Chronobiology & Sleep Research Facilities at the Brain & Mind Research Institute, The University of Sydney, are located on Level 5, 94 Mallett Street, Camperdown NSW. The Chronobiology & Sleep Group (CSG) is an internationally recognised research group investigating the neurobehavioural, neuropsychological and neurobiological activities of the circadian and sleep homeostatic systems. The aims of the CSG include the identification, prevention and management of sleep loss and circadian disruption associated with sleep and circadian disorders, insufficient sleep, circadian misalignment (shiftwork and jet lag), psychiatric and neurodegenerative disorders, as well as understanding normal sleep and circadian functioning.

Of particular interest to investigators is the connection between sleep disturbance and neurodegenerative disorders such as Parkinson's Disease (PD), Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), Frontotemporal Dementia (FTD) as well as late onset depression.

The Chronobiology & Sleep Research Facilities at the Brain & Mind Research Institute include the Chronobiology & Sleep Laboratory (CSL), which has been designed for 24-hour circadian and sleep studies, longer duration circadian and sleep/sleep deprivation studies, daytime assessments and overnight studies, as well as clinical studies.
The lab consists of four separate bedrooms and a performance testing room, as well as driving simulators and a range of equipment for physiological monitoring and assessment of subjects.

Patient information

There is 1-hour and 2-hour parking available on Mallett St and disabled parking out the front of the BMRI building. There is also all-day parking on Australia St.

Patients using public transport, can take a bus from Central Station: Railway Square, George St. Stand D, travels along Parramatta Rd, bypassing Missenden Rd. Patients can take the 413, 435, 436, 437, 438, 440, 461, 480, 483 or the metrobus. Alight at the first stop after Missenden Rd. This stop is located on the corner of Mallett St (outside a camping store).
Turn left into Mallett St and walk 300 metres. The BMRI at number 94 is on the left.

For further information and referrals phone Inger Quinn on 02 9114 0007 or email inger.quinn@sydney.edu.au, or fax 02 9114 0465

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CHRONOBIOLOGY

THE LAPS STUDY - LIGHT THERAPY TO IMPROVE ALERTNESS IN SHIFTWORKERS - (NHMRC - MULTICENTRE)

A/Prof Shantha Rajaratanam, Prof Ron Grunstein, Tracey Sletten

Summary
To test in a randomized controlled trial (RCT) the efficacy of a novel light-exposure intervention to improve alertness and neurobehavioural performance in night shift workers.

Inclusion criteria:

- Males and females
- Age 18-65 years working ≥ 5 night shifts per month for ≤ 12 h, with ≥ 6 h worked between 10pm and 8am, and ≥ 2 shifts occurring consecutively.

Exclusion criteria: Unstable medical or psychiatric conditions that may place the participant at risk due to study procedures (e.g. sleep deprivation, light exposure). Excluded medications include antipsychotics, illicit drugs

Contact
Suzanne Wellington, email sue.wellington@sydney.edu.au, or phone 02 9114 0262 or 02 9114 0259.

ASSESSING SLEEP-WAKE PATTERNS IN ADULTS – PI Prof Sharon Naismith

Sleep loss and circadian disruption are endemic in our global 24-7 society. Contributors to sleep loss and circadian disruption include increased work hours and shiftwork; sleep and other medical conditions; and family or social demands; often with more than one factor co-occurring. As a result, millions of individuals commonly experience reduced neurocognitive functioning with decreased alertness and increased fatigue, putting them at increased risk for errors, injuries, traffic accidents, personal conflicts and drug use. In addition, numerous alterations in 'normal' physiology occur, increasing the risk of numerous health complaints, including increased weight gain, cardiovascular disorders, mood disorders and mortality. Disruption to these two systems may also underlie other medical disorders (e.g., depression and other affective disorders), contributing to the occurrence and severity of symptoms.

Despite recommendations based on scientific evidence that adults should obtain 8 hours of sleep per night to maximise waking functions, sleep durations tend to be consistently less than this. In a study of more than 1.1 million Americans, approximately 20% reported getting 6.5 hours or less sleep per night. In Australia, chronic sleep restriction is also common, with around 18% of NSW adults reporting that they sleep 6 hours or less per night, as assessed by questionnaire.

In order to better understand the nature of the sleep restriction occurring in the local population, including the actual sleep durations and sleep-wake timing, we aim to objectively assess sleep-wake behaviour in adults living in Sydney using wrist actigraphy. In conjunction with this objective measure of sleep-wake timing, sleep duration and sleep quality, we will also collect subjective estimates of sleep durations and sleep quality using subjective sleep diaries. Participants will also complete a number of questionnaires regarding their sleep-wake patterns, general health and circadian preference.

These data will provide us with important information regarding typical sleep-wake behaviour in adults living in the local area. These data will also provide information on a 'healthy control' group for studies conducted in patient populations. This information will assist in our understanding of the role that changes in the sleep-wake and circadian systems play in disease severity and symptomatology that are disease specific, and separate from changes caused by lifestyle induced changes in sleep-wake duration and timing.

Contact
Sharon Naismith, email sharon.naismith@sydney.edu.au or Suzanne Wellington, email sue.wellington@sydney.edu.au, phone 02 91140262 or 02 91140259.

ASSESSING SLEEP-WAKE PATTERNS IN SCHOOL STUDENTS – PI Prof Sharon Naismith

Sleep is essential for learning and memory function, as well as being a time during which normal growth and development occur in adolescents. During the teenage years changes in the circadian system, resulting in changes in sleep-wake timing and sleep need occur, likely due to pubertal development. In addition, the teenage years is also the predominant time for the onset of many mood disorders, that may be preceded by significant changes in sleep-wake behaviour.

In order to better understand the nature of sleep-wake patterns and behaviour in this age group, including sleep length and sleep-wake timing, we aim to objectively assess sleep-wake behaviour in school aged children living in Sydney and attending a local school using wrist actigraphy and subjective sleep diaries. Participants will also complete a number of questionnaires regarding their sleep-wake patterns, general health and circadian preference.

In addition we are developing an educational program with various aspects aimed at teachers, students and parents that will be delivered as part of this project.

Contact
Sharon Naismith, email sharon.naismith@sydney.edu.au or Suzanne Wellington, email sue.wellington@sydney.edu.au, phone 02 91140262 or 02 91140259.

LONGITUDINAL ASSESSMENT OF SLEEP-WAKE PATTERNS IN SCHOOL STUDENTS DURING PUBERTAL DEVELOPMENT – PI Prof Sharon Naismith

Sleep is essential for learning and memory function, as well as being a time during which normal growth and development occur in adolescents. During the teenage years changes in the circadian system, resulting in changes in sleep-wake timing and sleep need occur, likely due to pubertal development. In addition, the teenage years is also the predominant time for the onset of many mood disorders, that may be preceded by significant changes in sleep-wake behaviour.

As an extension of our study examining sleep-wake patterns in school students, we aim to follow a group of students across a number of years to track changes in sleep-wake timing and sleep quality throughput pubertal development. At each assessment time point (12 months apart) we will assess sleep-wake behaviour using wrist actigraphy, subjective sleep diaries and a range of questionnaires relating to sleep, circadian rhythms and general health.

Contact
Sharon Naismith, email sharon.naismith@sydney.edu.au or Suzanne Wellington, email sue.wellington@sydney.edu.au, phone 02 91140262 or 02 91140259.

SLEEPING ON THE JOB: INCREASING ALERTNESS & PRODUCTIVITY IN THE WORKPLACE – PI Prof Sharon Naismith

Despite recommendations to sleep 8 hours per night for optimal performance during the day, many people regularly get less than 8 hours per night. Consequently, a daytime nap may be beneficial to maintain or increase alertness and performance across the day. Even in those who obtain 'adequate' night-time sleep, a daytime nap can have a positive effect on alertness, productivity and neurocognitive functioning during the working day. Few studies have focussed on the benefits of napping in non-shiftworking workers.

There is considerable interest in workplace napping, with a number of industries not involved in shiftwork seeking ways to maximise workers' alertness throughout the day, especially with extended work hours becoming common in many employment sectors.

We aim to investigate the effects a 30 minute nap has on alertness, productivity and memory in day-workers. We are also investigating people's subjective feelings about their nap sleep. This study is being conducted using a specially designed napping pod (MetroNaps), which creates a sleep conducive environment inside a semi-enclosed pod.

Contact
Sharon Naismith, email sharon.naismith@sydney.edu.au or Suzanne Wellington, email sue.wellington@sydney.edu.au, phone 02 91140262 or 02 91140259.

ENDOCRINE/ METABOLISM

THE CATCH-UP STUDY - PI A/Prof Peter Liu, Dr Roo Killick

Summary
To ascertain whether restorative sleep in chronic, intermittent, lifestyle- driven sleep restrictors is protective against the development of insulin resistance and subsequent diabetes. We also want to assess changes in neurocognitive function between restorative weekend sleep, sleep restriction and specific slow-wave sleep (SWS) deprivation.

Inclusion criteria:

- Males between age of 18 -50 years.
- Self-reported lifestyle-driven, chronic, intermittent sleep restrictors, who sleep longer on weekends ("catch-up" sleep) than during the working week.
- Good general health.

Exclusion criteria: Diabetes, sleep disorders, shift workers.

Contact
Roo Killick, email rookillick@woolcock.org.au, or phone 02 9114 0499 or Suzanne Wellington, email: sue.wellington@sydney.edu.au, phone 02 9114 0262 or 02 9114 0259.

THE SHIFTWORK STUDY – DOES SHIFTWORK INCREASE POSTPRANDIAL HYPERLIPIDEMIA? (NHMRC/CCRE) PI Dr Craig Philips, A/Prof David Sullivan

Summary
This study utilises a simulated shift work paradigm that compares the effects of day versus night shift work (three consecutive cycles of 12-hour shifts) on glucose and lipid metabolism. The study is designed to test whether wakefulness and ingestion of meals occurring out of phase with the body's circadian sleep cycle (as occurs during night shift) results in postprandial dysmetabolism, an important marker of cardiovascular risk. The study will target an overweight-obese and middle-aged group that are highly represented amongst shiftworker populations and who are already at increased CVD risk.

Inclusion criteria:
- Males and females
- Age 30-50 years
- BMI 25-35 kg/m2
- Non-shift workers.

Exclusion criteria: Hyper-Triglycerdemia (TAG>4mmol/dl), Impaired fasting glucose (>5.6 mmol/dL), Current shift worker, moderate or worse OSA (AHI>15) or treated OSA, history of cardiovascular, renal or metabolic disease including stroke, coronary heart disease, kidney disease and diabetes (Type 1 & 2), other comorbid sleep conditions (insomnia, sleep phase syndromes, narcolepsy) neurological or psychiatric disease that the investigators consider will alter normal sleep patterns.

Contact
Chris Miller, email c.miller.2@research.gla.ac.uk, or phone 02 9114 0262 or 02 9114 0259

THE CPAP ED² STUDY - DOES SLEEP APNOEA TREATMENT IMPROVE ENDOTHELIAL FUNCTION AND ERECTILE DYSFUNCTION? (NHMRC) A/Prof Peter Liu, Kerri Melehan

Summary
The effect of CPAP on erectile and endothelial dysfunction in men with obstructive sleep apnoea and erectile dysfunction. To evaluate the separate and combined effect of continuous positive airway pressure (CPAP) and/or nightly medium dose Vardenafil on erectile and endothelial function in impotent men with obstructive sleep apnoea.

Inclusion Criteria
- Men aged 18-65
- Moderate-severe OSA. RDI≥20 & ODI(3)≥15
- Erectile dysfunction defined by IIEF-EF for at least 6 months
- Stable heterosexual relationship for at least 6 months

Exclusion Criteria
Severe OSA requiring immediate treatment, treatment of erectile dysfunction within the last month, concurrent treatment with nitrates or nitric oxide donors, irreversible erectile dysfunction (e.g., post radical prostatectomy), severe renal or hepatic impairment, medications that potently inhibit the cytochrome p-450 isoenzymes (e.g., HIV protease inhibitors) & CYP3A4 inhibitors, history of unstable angina, hypotension (resting systolic BP <90), uncontrolled hypertension (>170/110), heart failure, recent history of stroke, arrhythmia or MI, significant respiratory disease, diabetes or who smoke that is likely to interfere with the evaluation of patients safety and/or efficacy parameters, other significant medical condition, shiftworkers or patients with irregular sleep / wake routine, for overnight blood sampling – blood donation within last 3 months.

Study Procedure
- 5 visits (includes 2 x PSG's)
- Overnight blood sampling & NPT optional
- Partner inclusion optional, does not exclude participant

Contact
Kerri Melehan, email kerrim@woolcock.org.au, or phone 0408 417 520 or 9114 0498 or 9515 7776 or Suzanne Wellington, email sue.wellington@sydney.edu.au, or phone 02 9114 0262 or 02 9114 0259.

THE INFLATE STUDY - ENDOCRINE AND METABOLIC EFFECTS OF NSAID THERAPY ON OVERWEIGHT, DIABETES AND HYPOGONADISM (NHMRC/CCRE) - A/Prof Peter Lieu, Liz Machan, Camilla Hoyos

Summary
Examining the effects of non-steroidal anti-inflammatory drug therapy on blood sugar control, hormones, quality of life and reproductive and sexual health in men with OSA.

Inclusion Criteria
- Men aged 18-65
- BMI ≥ 27 kg/m2
- RDI ≥ 5
- Waitlisted or refuses CPAP
- Testosterone < 10 nmol/l

Exclusion Criteria
- Chronic conditions (diabetes, liver/ kidney disease, cardiovascular disease)
- Current smoker
- History of drug and alcohol abuse
- Significant previous exposure to CPAP
- Current use of NSAID's

Study Procedure
- 3 months (5 x short visits & 2 x PSG's)

Contact
Liz Machan, email elizabeth.machan@sydney.edu.au, phone 02 9114 0456

THE CAPER STUDY - CONSEQUENCES OF APNOEA ON THE PARTNER AND EFFECTS ON REPRODUCTION A/Prof Peter Liu, Kerri Melehan, Camilla Hoyos

Summary
Examining the effects of CPAP on blood sugar control hormones, quality of life and reproductive and sexual health in men with OSA, and the effect of CPAP use by the man on the female partner

Inclusion Criteria
- Heterosexual couple, man has OSA
- Aged 18-65
- Couple share a room/bed
- Male RDI > 20
- Male ODI >15
- Relationship > 6 months
- Agree to not smoke for visits

Exclusion Criteria
- Uncontrolled medical conditions
- Males with severe OSA
- Shiftworkers
- Females with a high probability of OSA (MAPI ≥ 0.5)

Study Procedure
- 3 months (5 x short visits & 2 x PSG's)

Contact
Kerri Melehan, email kerrim@woolcock.org.au, or phone 02 9114 0498

INTERACTIONS BETWEEN PROTEIN LEVERAGE, VARIETY, AND DIETARY CARBOHYDRATE AND FAT CONTENT IN THE CONTROL OF ENERGY INTAKE IN HUMANS – (NHMRC PROJECT GRANT 1003225) – Prof Stephen Simpson and Prof Arthur Conigrave (The University of Sydney)

Summary
The protein leverage hypothesis suggests that food consumption in humans, like other animals, is adjusted to maintain a protein target. We hypothesize that there are interactions between sensory variety, carbohydrate vs fat and regulatory responses controlling protein intake. We propose to use an experimental design that will first test the potential of fat versus carbohydrate to accentuate the effect of a dilution in dietary protein and we will then test the effect of variety. Therefore

the study will consist of 2 separate studies. Each study will be will be four, 5-day treatment periods. All of which will be experienced by each subject in a randomized order.

Recruitment target: n= 60 (30 for each study)

Length of study:
1. Short screening visit (<1hr).
2. Initial investigation day 3. 4 x 5 day study periods

Inclusion Criteria
Females or Males, 18-55 years balanced across treatments; BMI 20-25kg m-2.

Exclusion Criteria
Pregnancy or planning pregnancy, breastfeeding, menopausal symptoms or post-menopausal status, known diabetes, known unstable or untreated elevated blood pressure or cholesterol, cardiovascular disease, chronic inflammatory conditions, medications that may interfere with glucose metabolism, smoking, alcohol consumption above current NHMRC guidelines, allergy or intolerance to any of the intervention foods, irregular eating patterns or eating disorder, following a weight reducing diet. Vegetarians and vegans will be excluded to aid preparation of covertly manipulated diets.

Study Procedure
After a screening interview and completion of a questionnaire, participants will attend for an initial day of investigations and then four, 5-day treatment periods with at least 10 days between each visit. During each treatment period participants will be provided with ad libitum food. For each 5-day period participants will spend the days and nights at the Woolcock Institute of Medical Research sleep centre (Glebe Point Road, Glebe NSW 2037) under continuous supervision. Subjects will be tested in single-sex groups of up to four. The group will stay together throughout the full experiment and all members of each group will experience the same treatment order.

Initial investigation day
Participants will arrive after an overnight fast, bringing a 4-day food diary and 24-h urine sample. Prior instruction will be provided in these tasks. Questionnaires will be completed to assess medical history, eating behaviour, sleeping habits and physical activity. Measures will be taken of height, weight, waist circumference and blood pressure.

Experiment week
Day 1: Up to four participants will arrive from home after an overnight fast bringing with them a 4-day food diary, an Actiwatch that has been worn for 4 days and a 24 hour urine collection. Weight, waist circumference and blood pressure will be measured. A continuous glucose monitor will be inserted and worn until day 5, an Actiwatch will also be give to participants to wear throughout the study. Fasting blood samples will be taken for biochemical analysis (Table 1). Food will be provided ad libitum in excess and subjects invited to eat throughout the day and to keep a food log of when and what they eat. They will spend an hour in the afternoon on a supervised walk. At other times they will be confined to the Woolcock.

Day 2: Food and exercise will be provided as day 1 and subjects will be asked to continue the food log.

Day 3: Food and exercise will be provided as day 1 and subjects will be asked to continue the food log.

Day 4: Food and exercise will be provided as day 1 and subjects will be asked to continue the food log. The first 24 h urine collection will begin. Participants will be asked to complete visual analogue scales (VASs) for the measurement of subjective appetite for sweet and savoury foods throughout the day.

Day 5: The 24 h urine collection will be completed. The measures performed on day 1 will be repeated. The continuous glucose monitor and Actiwatch will be removed.

Subjects will be offered a free choice breakfast.

Days 1 to 5 will be repeated on three further occasions with at least 10 days intervening.

Contact
Alison Gosby, email alison.gosby@sydney.edu.au, or phone 02 9036 6262.

INSOMNIA/ DEPRESSION/ NEUROLOGICAL DISORDERS AND SLEEP

EARLY SLEEP CBT INTERVENTION TO REDUCE DEPRESSIVE SYMPTOMS IN NEW MOTHERS

PI A/Prof Delwyn Bartlett, Liora Grunstein

Inclusion criteria

- Ability to understand and speak English fluently.
- New mothers booked for Pre-Natal classes at RPA Women & Babies.

Exclusion criteria

Inability to understand or speak English fluently. Individuals who do not understand English will be unable to understand the slide presentation or written material. The questionnaires have only been validated and normed in individuals who speak English fluently.

Study Procedure

Participants will be asked to complete a number of questionnaires (listed below), designed to gauge mood, sleep habits, levels of tiredness and expectations of experience with their newborn.

Participants will be asked to keep a sleep diary for 7 days before they have their baby, and again 6 weeks and 3 months after delivery. A small number of participants will also be asked to wear an actigraphy device (size of a watch) on their wrist.

A number of participants will be randomised to a cognitive behavioural therapy intervention group, where they will be asked to attend with their partner (optional) and participate in a 1.5 hour educational session (slide presentation). This session will contain information on normal sleep; sleep during pregnancy; sleep in the first few weeks after delivery (highlighting the fact that parents generally lose 1.5 hours of sleep every night in the first week after delivery). The session will also include information on the baby's sleep 'in utero' (increased REM or dream sleep); establishment of baby's sleep pattern which occurs at approximately three months; and generally what to expect in relation to the participants sleep and their baby's sleep.

Participants will be given a copy of the slide presentation to take with them and a number of booklets which will give them strategies to enable better sleep onset or return to sleep after feeding their baby.

Participants randomised to the treatment as usual group will also receive written information on sleep during late pregnancy and in the first three months. In addition, they will be given a number of booklets which will give them strategies to enable better sleep onset and return to sleep after feeding their baby. They will also be offered the opportunity to attend an in depth session on sleep management for them and their baby at the completion of the study.

A researcher will contact the participant again approximately six weeks after delivery and provide the set of questionnaires again, along with the Edinburgh Questionnaire. The participant will also be asked to keep a sleep diary for one week.

Thirteen weeks after delivery a researcher will contact the participant once more and ask them to complete the questionnaires again and to keep a sleep diary for another week. If the participant was asked to wear an actiwatch before the baby's birth, the participant will again be asked to wear it for a week at this three month time point.

Questionnaire Utilisation

The Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), the Depression, Anxiety, and Stress Scale (DASS), the Being a Mother & Bonding Scale (BaMB), the Multidimensional Assessment of Fatigue (MAF) questionnaire and the Edinburgh Post Natal Depression Scale (EPDS) will be used through the study.

Description of the Home Monitoring Device

An Actiwatch is a wristwatch like device which has an accelerometer (a motion detector) which defines sleep as reduced movement under a given threshold and allows for the measurement of sleep/wake patterns over a number of days.

Contact:

Liora Grunstein, email liora.grunstein@sydney.edu.au, or phone 02 9114 0495 or Suzanne Wellington, email sue.wellington@sydney.edu.au, or phone 02 91140 262 or 02 9114 0259.

COMPARISON BETWEEN SLEEP EDUCATION AND COGNITIVE BEHAVIOURAL THERAPY FOR INSOMNIA (CBT-I) IN CO-MORBID INSOMNIA AND DEPRESSION.

PI A/Prof Shantha Rajaratanam, Damon Ashworth

Summary

Insomnia and Depression share many common features such as low energy, fatigue, poor concentration and sleep difficulties. Insomnia is not just a symptom of depression however, and this is why insomnia symptoms remain nearly 50% of the time through antidepressant treatment. The objective of this study is to treat the sleep disturbances in individuals with depression and insomnia (whose symptoms have not remitted through at least 6-weeks of antidepressant treatment) with 4 sessions of CBT-I or sleep education. The aims are to improve the participant's quality of sleep and reduce both their insomnia and depression severity.

Recruitment target: n = 40

Length of study:

1. Short screening visit (60-75 min).
2. Treatment – 4 visits of 50 min duration over an 8 week period (1 visit/ fortnight).
3. 3-month follow-up assessment (50 min duration).

Location:

Monash University Clinical Psychology Centre, Notting Hill, Melbourne.

Design:
Randomised Controlled Trial.

Inclusion Criteria
Males and females between the ages of 18-65 with Major Depressive Disorder and chronic insomnia who have been prescribed with and have adhered to standard antidepressant (SSRI) treatment for at least 6 weeks.

Exclusion Criteria
Use of medication for insomnia in the 14 days prior to the screening visit; Other ongoing types of treatment (including over-the-counter medications or herbs) or therapy (including alternative therapy) of claimed efficacy for depression or insomnia; Electro-convulsive therapy (ECT) in the prior year; Current active suicidal potential or psychotic features; Diagnosis of seasonal affective disorder or major depressive disorder (MDD) with a seasonal pattern; Other co-morbid psychiatric conditions, Conditions incompatible with standard antidepressants (SSRIs); Current diagnosis of any other primary sleep disorder or any uncontrolled medical conditions; inadequate English language fluency.

Study Procedure
After obtaining informed consent and assessing for eligibility at a screening session, participants will be required to complete baseline questionnaires on their mood, sleep and daytime functioning and monitor their sleep-wake behaviour over a two-week baseline period using sleep-wake diaries and actigraphy (movement monitor that differentiates between sleep and wake).

Participants will then be randomly allocated to either: a) CBT-I multimodal treatment or b) Information only control. Each group will be given the same information, but the CBT-I group will receive one-on-one face-to-face feedback about the information presented and their sleep. Information presented in each treatment session will include sleep education, stimulus control and sleep restriction, dysfunctional beliefs and attitudes to sleep and mindfulness exercises. Sleep behaviour will be monitored and adapted to the individual during sessions.

Post-treatment and follow-up:
Measures will be gathered at the end of the 8-week treatment and at 3-month follow-up to determine changes throughout the study. The CBT-I sessions will then be offered to the information only control group, although data will not be collected for the study during this time.

Contact:
Damon Ashworth, email damon.ashworth@monash.edu or phone 03 9905 3952.

ACTIGRAPHIC ASSESSMENT OF SLEEP-WAKE BEHAVIOUR IN PATIENTS WITH BIPOLAR DISORDER AND DEPRESSION - PI Prof Sharon Naismith

The aim of this study is to characterise and track sleep-wake behaviour in patients with bipolar disorder, studied at various phases of illness.

This study assesses sleep-wake behaviour (timing and quality) across a 2 week period in patients with bipolar disorder, using actigraphy and sleep diaries. Patients also complete a number of questionnaires relating to their sleep and chronotype.

In the sleep diary, participants will be asked to record what time they went to sleep each night, what time they awoke the next day, how long they took to fall asleep, if they woke across the night, and to rate their sleep quality.

Contact
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IDENTIFYING POTENTIAL BIOMARKERS FOR EARLY INTERVENTION TO REDUCE RATES OF ONSET AND RELAPSE IN PATIENTS WITH BIPOLAR DISORDER - PI Prof Sharon Naismith

This study will assess parameters of the sleep-wake and circadian systems in an attempt to define biomarkers of onset of symptoms in at risk individuals and of relapse in patients with bipolar disorder. One target biomarker is the phase angle between melatonin onset and sleep onset, sleep offset and temperature nadir.

Participants will complete at home actigraphy and light assessments, and then complete two overnight sessions in the lab with polysomnographic assessment of sleep. Participants will then complete a third night where salivary melatonin levels and core body temperature will be assessed to obtain an assessment of circadian phase. The phase angle relationship between the dim light melatonin onset (DLMO) and sleep and temperature variables will then be investigated for changes in circadian and sleep-wake stability, which may then be used as an early biomarker of changes in symptoms and potential relapse or onset of symptoms.

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ZIPRASIDONE & SLEEP-WAKE INTERVENTIONS FOR PATIENTS WITH BIPOLAR DISORDER (funded by Pfizer) – PI Prof Sharon Naismith

This is a single arm study investigating the effects of combining ziprasidone treatment and interventions to reentrain the circadian system and improve sleep-wake timing and sleep consolidation and quality.

At home sleep-wake activity and light exposure will be assessed using wrist actigraphy and daily sleep logs. Actigraphic data will be collected during a baseline period, immediately prior to removing participants from their current medication and commencing them on ziprasidone, during the period of stabilisation on ziprasidone and for 4 weeks following stabilisation.

At 3 months and 6 months following the stabilisation on ziprasidone, participants will again wear the actigraphs and complete sleep diaries for a period of 4 weeks each.

The primary aim of this study is to quantify sleep-wake timing and sleep quality in patients with bipolar disorder who are experiencing an episode of mania or depression and commencing treatment with ziprasidone (80-160mg per day)

The secondary aims of this study are to:

- examine the effectiveness of combining administration of ziprasidone with education on sleep-wake activity and behavioural interventions to improve sleep-wake behaviour on symptoms and recovery in the short term (4 weeks post commencement of stable treatment with ziprasidone);
- examine the effectiveness of combining administration of ziprasidone with education on sleep-wake activity and behavioural interventions to improve sleep-wake behaviour on symptoms and recovery in the long term (3 and 6 months post commencement of stable Treatment with ziprasidone).

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QUETIAPINE & SLEEP-WAKE INTERVENTIONS FOR PATIENTS WITH BIPOLAR DISORDER – PI Prof Sharon Naismith

This study will investigate alterations in the circadian system and sleep-wake behaviour in patients with diagnosed bipolar disorder in conjunction with starting on Quetiapine. Patients will be recruited during an episode for patients in the depressive phase, and immediately following stabilisation for patients in the manic phase. Participants will commence treatment of Quetiapine, combined with education on sleep-wake activity and behavioural interventions to improve sleep-wake behaviour on symptoms.

We will track changes in circadian timing and sleep-wake behaviour across a period of 3-6 months in these patients, to assess changes in the circadian and sleep-wake systems and how these relate to subjective and objective reports of symptoms, and determine if a relationship between the degree of circadian and/or sleep disturbance or remission and the time to relapse exists. These investigations will be conducted both at home (using wrist actigraphy to monitor sleep-wake behaviour and sleep diaries) and in the lab (using polysomnography to assess sleep and melatonin profiles to assess the circadian system).

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CIRCADIAN RHYTHMS AND METABOLIC FUNCTIONING IN SCHIZOPHRENIA – PI Prof Sharon Naismith

Sleep-wake disturbances and disruption to the circadian timing system are commonly reported in patients with schizophrenia. In addition to the negative effects on mood, alertness and neurocognitive functioning, sleep loss and circadian disruption are also associated with a number of physiological changes and negative health outcomes. For example, sleep loss and circadian disruption have both been associated with changes in metabolic function and weight control. Sleep loss and short sleep durations have been associated with increased risk of weight gain, obesity and metabolic disorders such as diabetes type-2.

Although a number of medications used in the management of schizophrenia are reported to increase weight gain as side effects, schizophrenia alone is reported to increase weight gain and increase the risk of metabolic disorders, independent of the medications.

In a series of studies we aim to investigate the sleep-wake and circadian changes that occur in schizophrenia, and determine if these changes may form part of the underlying mechanisms that contribute to the metabolic changes associated with this disorder.

Initially we will investigate sleep-wake behaviour in patients with schizophrenia using actigraphy and sleep diaries across a number of weeks. We will then assess circadian phase in a sub-set of these patients, using salivary levels of the pineal hormone melatonin, to determine their internal circadian timing. Further investigations will include assessment of a range of compounds related to metabolic function, including glucose, insulin, leptin and ghrelin, as well as other indicators of weight gain and general health in patients admitted for treatment.

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SLEEP-WAKE DISTURBANCES IN OLDER PEOPLE WITH NEUROPSYCHIATRIC DISORDERS – PI Prof Sharon Naismith

Sleep-wake disturbances are commonly found in patients with neurodegenerative disorders, including Parkinson's Disease (PD), Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), late onset depression and Frontotemporal Dementia (FTD). These disturbances are often associated with neuropsychiatric (e.g. cognitive, psychiatric) symptoms, raising the possibility of a common underlying pathological correlate. Although the fundamental cause of these sleep-wake disturbances remains unclear, it may reflect disruptions within the circadian system, a regulator of sleep-wake cycle timing. However, in neurodegenerative disorders, no formal studies have concurrently examined both sleep and circadian disturbance using the techniques of polysomnography (PSG), actigraphy and assessment of melatonin profiles (as a circadian marker) in association with detailed neurological and neuropsychological assessment. This study will objectively evaluate circadian rhythms and sleep-wake physiology in a range of differing older patient cohorts as well as in healthy controls to examine the role of the circadian system in these disorders. Specifically, the aims are to;

- Determine whether specific neurodegenerative diseases have distinct patterns of circadian disturbance as recorded by their endogenous melatonin levels;
- Describe the relationship between circadian disturbances and the profile of sleep disturbance as recorded by the techniques of polysomnography and actigraphy within and between specific disease groups; and,
- Determine whether circadian and sleep-wake disturbances are associated with neuropsychiatric symptoms in neurodegenerative disease.

Participants' sleep-wake patterns and light exposure will be assessed at home using actigraphy and a light sensor. Further assessment of sleep using PSG will be conducted across two nights in the lab, followed by a third overnight testing session for collection of salivary melatonin levels, to assess circadian phase, and neurocognitive performance assessments.

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CIRCADIAN & SLEEP-WAKE PATTERNS IN PATIENTS WITH MULTIPLE SCLEROSIS – PI Prof Sharon Naismith

Patients with MS suffer with prominent, although likely under-recognised, cognitive dysfunction which can have serious impact on their functioning, especially in the workplace. Additionally, debilitating fatigue is an extremely common symptom in MS patients. The pathophysiology of early cognitive dysfunction and fatigue in MS is largely unknown and therapies, largely designed to promote wakefulness, are poorly effective. Questionnaire-based studies indicate that sleep disturbance is a frequent manifestation of MS, however formal studies of circadian rhythms in this population are lacking. Exploring the relationship between disturbances of circadian rhythm, fatigue and cognitive dysfunction in MS will provide new pathophysiological data and, potentially, avenues for the development of novel therapies to combat these symptoms.

The present study aims to evaluate circadian rhythms in people with MS compared to healthy controls. The study will have the following aims:

- To test the hypothesis that, compared with healthy controls, patients with MS will show differing and characteristic patterns of delayed circadian phase, as assessed by salivary dim light melatonin onset (DLMO);
- To assess the relationship between circadian system disturbance and cognitive decline in these patient groups;
- To assess the relationship between circadian system disturbance and psychiatric disturbance in these patient groups;
- To determine the relationship between circadian rhythm disturbance and fatigue in MS patients.
- To determine the predictive capacity of circadian rhythm changes for cognitive decline and disease progression longitudinally.

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THE INSOMNIA 100 STUDY - PI Prof Ron Grunstein, A/Prof Delwyn Bartlett, Chris Miller

Summary
We wish to recruit 100 individuals suffering from Insomnia to take part in a sleep research study at the Woolcock Institute of Medical Research, University of Sydney.

The objective of this study is to investigate differences within certain types of Insomnia. This study will evaluate Insomnia sub types through a routine diagnostic sleep study, questionnaires, computer based assessment tasks, and a blood sample.

Interested volunteers will receive a short telephone interview to determine suitability for the study. If suitable they will be asked to complete some brief questionnaires concerning sleep and wear an actiwatch. We will then invite them to attend an overnight sleep study assessment.

Inclusion Criteria
Males and Females between the ages of 25 – 55 suspected to be suffering from chronic Insomnia.

Exclusion Criteria
Use of medication for Insomnia; current diagnosis of any other primary sleep disorder or any uncontrolled medical conditions; Inadequate English language fluency.

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OBSTRUCTIVE SLEEP APNOEA/ CPAP/MAS/ RESPIRATORY

BRAIN BIOMARKERS OF PERFORMANCE IN OBSTRUCTIVE SLEEP APNOEA - (NHMRC PROJECT GRANT 1028624) - Prof Ron Grunstein, Dr Keith Wong, Prof Caroline (Lindy) Rae (UNSW), Prof Doug McEvoy (Flinders)

Summary
This is a 3 year, cross-sectional, single site study of 85 patients with moderate to severe OSA undergoing assessment of neurobehavioural function during 28 hrs of extended wakefulness. We will perform a number of assessments at baseline to see which tests can potentially be used as biomarkers of neurobehavioral dysfunction (impaired driving).

Recruitment target: n= 85

Length of study:
1. Short screening visit (<2hrs).
2. Test visit – arrive 6pm Day 1 leave 10am Day 3 (i.e., spend 2 consecutive nights in the laboratory)

Design: Cross sectional

Inclusion Criteria
- Males and females
- Age 30-65
- Weight BMI<35
- Polysomnography confirmed OSA (Apnoea Hypopnea Index >15 events/hr)
- Oxygen Desaturation Index (ODI) 4% >10 drops/hr
- Not been treated for OSA (continuous positive airway pressure machine or mandibular advancement splint) for 6 months.

Exclusion Criteria
- Clinically significant co-morbidity
- Uncontrolled medical conditions e.g. cardiac failure, hypertension, hypercapnia; claustrophobia or unable to have MRI/MRS due to metal fragments or other foreign bodies
- History of head injury or psychiatric/ neurological disorder (including stroke)
- Use of central nervous system active agents
- Heavy alcohol consumption (>40g daily)
- Current shift-worker
- Professional drivers.

Study Procedure
After obtaining informed consent and determining eligibility during a screening visit, participants return for a test visit. The test visit consists of standard sleep centre assessments and questionnaires (BMI, Epworth Sleepiness Scale etc) and a baseline sleep study followed by neuroimaging the next morning and then 28 hours of extended wakefulness with detailed assessment. One week of actigraphy (movement monitor that differentiates between sleep and wake, and records ambient light levels) and sleep-wake diary and indoor-outdoor activity logs, will be performed prior to the test visit to measure sleep hours and activities at home, and participants will be advised to observe regular sleep hours with 8-hours in bed.

The study will take place at the ACCESS centre, a 5 bedroom purpose-built, controlled environment for human sleep and circadian experimentation with full noise, vibration and light control, and area for individual neurobehavioural testing. Magnetic resonance imaging will be performed at NeuRA, Randwick (20 min by taxi). The repeated neurobehavioural performance testing during the 28-hour extended wakefulness period include:

- A 90 minute computerised driving simulator task.
- Resting awake EEG during a 7 minute Karolinska Drowsiness Test.
- Subjective sleepiness assessed by questionnaire.
- Computerised performance tests:
- Working memory (N-back 1,2,3)
- Visuomotor skills (Digit Symbol Substitution Task)
- Vigilance (Psychomotor Vigilance Task)
- Event Related Potentials (ERP is an EEG based measure of brain activation in response to stimuli) during auditory odd-ball and visual working memory stimuli.
- EEG and heart rate variability will be continuously measured throughout the 28 h of extended wakefulness using portable devices.

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THE PHENOMAS STUDY -MULTI-MODAL PHENOTYPING IN OBSTRUCTIVE SLEEP APNOEA FOR PREDICTION OF ORAL APPLIANCE TREATMENT OUTCOME (NHMRC) - Professor Peter Cistulli

Summary: Mandibular Advancement Splints (MAS) can be an effective treatment for OSA in around two thirds of patients but the inability to preselect these patients is a barrier to use. Previously developed prediction models have shown reasonable success but predictive value tends to degrade on prospective validation. This may be due to the multifactorial nature of the upper airway response to MAS treatment. This study aims to phenotype patients using a range of assessments of upper airway structure and function and combine all assessments in a prediction model for treatment outcome. The objective of the research is to develop a clinically useful method for the prediction of treatment response to oral appliances in patients with OSA derived from multimodal assessments.

Recruitment target: n= 160 (80 males, 80 females, particularly need to recruit females)

Length of study: 8-12 weeks

Design: Interventional outcome prediction study

Inclusion Criteria
- age >18 years
- OSA defined by polysomnography (AHI >10/hour), within the last 6 months

Exclusion Criteria
- Central sleep apnoea
- Necessity for immediate therapy (e.g. sleep drivers)
- Co-existing sleep disorder (e.g. narcolepsy, shift work)
- Contraindications to oral appliance therapy (periodontal disease or dental caries, less than 10 teeth per dental arch, exaggerated gag reflex)
- Age <18 years
- Regular use of sedatives, narcotics, or psychoactive drugs
- Pregnant or breastfeeding

Study Procedure
- Approximately 4 visits as detailed below
- MAS assessment - at Sydney Dental Hospital to assess eligibility for study (includes a cone-beam CT). If the participant meets the dental criteria, impressions will be taken to manufacture the MAS (approx 2 weeks for manufacture).
- MAS fitting - at Sydney Dental Hospital to ensure fit of the splint.
- Phenotyping assessment - at Royal North Shore Hospital. A 1.5 to 2 hour visit (after issue but before regular use of the splint) to measure:
- Demographic data
- Medical history
- Anthropometric data
- Nasendoscopy
- Flow volume curves
- Nasal Resistance
- Craniofacial photography
- MAS titration period - 4-8 weeks - use of the splint every night with incremental advancement of the splint
- Final dental visit to ascertain optimal treatment advancement
- PSG at RNSH/Woolcock with the splint in situ to assess efficacy

Patients are entitled to keep the MAS on completion of the study if clinician deems this appropriate at follow-up.

Contact:
Amanda Greenwood, email: amanda.greenwood@sydney.edu.au, or phone 02 9926 5542.

OXYGEN AS SECOND-LINE THERAPY FOR OBSTRUCTIVE SLEEP APNOEA – PI Dr Keith Wong, A/Prof Brendon Yee, Dr David Wang, Dr Garrick Don, Prof Ron Grunstein.

Summary:
We aim to develop alternative treatments in patients refusing CPAP therapy. We hypothesize that 2 months of low-flow oxygen compared with room air, each delivered via nasal cannulae will improve sleep-disordered breathing, hypoxia during sleep, symptoms and maladaptive cardiovascular response in patients with OSA refusing CPAP treatment. Secondly, we hypothesize that patients with higher ventilatory loop gain will derive a greater benefit (reduction in apnoea-hypopnoea index) from oxygen therapy.

Inclusion Criteria:
- Aged 18-70 years
- OSA (apnoea-hypopnoea index >15/hour)
- Refused or intolerant of CPAP therapy

Exclusion Criteria:
- Current alternative therapy for OSA (i.e. MAS)
- Hypoxaemia (SpO2 <95%)
- BMI >38kg/m2
- Severe COPD or other lung disease
- Uncontrolled cardiac disease
- Participant or household member a smoker
- Severe nasal occlusion

Study procedure:
Participants will attend the Sleep Laboratory at Royal Prince Alfred Hospital for 2 visits. Initial visit testing will include:

- Pittsburgh Sleep Quality Index
- Epworth Sleepiness Scale
- Hypercapnic, hyperoxic & isocapnic, hypoxic ventilatory response testing
- Pseudorandom binary stimulation assessment of ventilatory loop gain
- 24h urinary catecholamine measurement
- Blood pressure monitoring
- Cranial Doppler ultrasound bubble studies to assess for evidence of patent foramen ovale
- Full overnight diagnostic polysomnography

Participants will then be randomised to receive 2 months of oxygen therapy or placebo delivered through identical commercial floor concentrators. The above variables will then be assessed again following the intervention.

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SLEEP PHARMACOTHERAPY

THE DEAR STUDY - DIET EXERCISE AND ARMODAFINIL - (NHMRC)
PI Prof Ron Grunstein, Dr Nathaniel Marshall

Summary
Diet, Exercise and Armodafinil for sleep apnoea patients who cannot use standard treatments.

The purpose of the study is to treat the daytime sleepiness with Armodafinil while reducing OSA severity graduallywith lifestyle modification.

Recruitment target: n= 130 patients

Length of study: 12 months

Design: Randomised controlled factorial clinical trial. Patients are randomised to armodafinil or placebo and are also randomised to one of two diets

Inclusion criteria (outline):
- Males & Females aged 18-70 years.
- General or central obesity; BMI≥27 but less than 40kg/m2 or waist circumference ≥80cm for women and ≥94cm for men.
- Moderate-severe and symptomatic OSA; (Apnoea Hypopnea Index (AHI) ≥ 15/hr with concomitant daytime sleepiness ESS≥10 or clinical report of disturbing daytime sleepiness).
- Must have rejected CPAP and MAS within the past 2 years.

Exclusion criteria (outline):
- Current use of device based treatment OR upper airway surgery within 6 months.
- Cognitive impairment/ Psychiatric disorder / Physically unable to participate/ other sleep disorder/night shift-work.
- Excessively sleepy patients at increased risk for driving-related accidents requiring immediate treatment.
- Previous use of modafinil or armodafinil.

Study Procedure
- 10 visits over a 12 month period including 3 overnight stays.
- Study visits involve: PSG, blood tests, anthropometry, neurocognitive tests and questionnaires to be completed on a computer, a driving simulator, body composition scanning (DXA and BIA), actigraphy, patients required to keep a daily diary regarding diet, exercise and sleep.

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THE MOSA STUDY MODAFINIL AND RESIDUAL SLEEPINESS – (NHMRC)
PI Prof Ron Grunstein, Dr Nathaniel Marshall

Summary
This pilot study aims to assess Modafinil's efficacy to improve parameters of daytime sleepiness and neurocognitive ability in untreated patients with mild to moderate OSA.

Inclusion criteria:
- Males aged 18-70.
- Willingness to participate documented by written informed consent. Able to understand, participate and comply with the requirements of the study procedures.
- Diagnosed OSA by night polysomnography (PSG) and having an apnea-Hypopnea Index (AHI) ≥5, ≤ 30. PSG results will only be accepted if they have occurred ≤ 6 months prior to the Screening visit.
- Refuse or cannot tolerate a continuous positive airway pressure (CPAP) device and/or a mandibular advancement splint (MAS).
- ESS ≥ 10 at Screening.
- Absence of significant co-morbidities.
- Fluent in English and able to comply with procedures (including normal motor function in dominant hand to operate computer terminal, and adequate corrected vision).

Exclusion criteria:
- Previous cardiovascular accident (CVA), head injury, colour blindness.
- Previously diagnosed psychological disorders, such as anxiety disorder, major depression, epilepsy, mania or psychosis.
- Patients with significant respiratory or neurological disease that is likely to interfere with the evaluation of the patient's safety and/or efficacy parameters,
- History of unstable hypertension, coronary heart disease or myocardial infarction,
- History of significant heart disease or, other significant heart manifestation in association with central nervous system stimulant use.
- Alcohol consumption: ≥ 4 standard drinks per day and consumption of xanthine-containing beverages (i.e. tea, coffee, or cola) comprising usually more than 4 cups or glasses per day.
- Use, or misuse, of substances of abuse.
- Current psychotropic drug use, such as methylphenidate; clomipramine; and, monoamine oxidase inhibitors.
- Concomitant medications that inhibit or are metabolised by cytochrome p-450 isoenzymes and other hepatic enzymes. These include, diazepam, phenytoin, propranolol, tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), warfarin, phenytoin, steroidal contraceptives, cyclosporin, theophylline, inducers or of CYP3A4 (e.g.carbamazepine, phenobarbital (phenobarbitone), rifampicin) and inhibitors of CYP3A4 (e.g. ketoconazole, itraconazole),
- Patients with severe renal or hepatic impairment, including patients with evidence of active liver disease (levels of AST, ALT and/or alkaline phosphatase >2x the upper limit of the normal range (ULN) and patients with impaired renal function as evidenced by a creatine value > 1.2x ULN.
- Patients with abnormal Thyroid function, including patients with evidence of Serum thyroxine (T4)

outside the normal range 4.6-12ug/dl, Serum Triiodothyronine (T3) outside the normal range 80-180 ng/dl and Serum thyrotropin (TSH) outside the normal range 0.5-6uU/ml.
- Patients who have used Modafinil in the past.
- Daytime blood pressure >160mmHg />100mmHg at the baseline visit.
- Treatment with CPAP within the last 3 months.
- Patients who have participated in a clinical trial within the last 60 days.
- Shift workers or patients with an irregular sleep/wake routine.
- Other diagnosed sleep disorders (e.g., Restless legs, Insomnia).

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THE CHOSA STUDY - CHRONOTHERAPY FOR HYPERTENSION IN OBSTRUCTIVE SLEEP APNOEA - Prof Ron Grunstein, Dr Craig Phillips, Dr Philip Lee

Summary

Chronotherapy is the "purposeful timing of medications, whether or not they utilise special drug release technology to proportion serum and tissue concentrations in synchrony with known circadian (and sleep/wake) rhythms in disease processes as a means of enhancing beneficial outcomes and/or attenuating or averting adverse effects."

This study aims to improve blood pressure control in OSA patients with hypertension (HT-OSA) by altering the timing of antihypertensive medication (Perindopril) ingestion. The study will evaluate the separate and combined effect of Perindopril taken once daily in the morning or at bedtime, and continuous positive airway pressure (CPAP) to optimise hypertension control in men or women with Hypertension and Obstructive Sleep Apnoea (OSA).

Inclusion Criteria

- Males & Females aged 18-65 years.
- Grade 1 or 2 hypertension (SBP between 140 and 179 mmHg and/ or DBP between 90 and 109 mmHg) based on Office BP.
- Less than 3 Anti-Hypertensive Medications that does not include an
- Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin
- Receptor Blocker (ARB).
- Moderate-severe OSA (Apnoea Hypopnea Index (AHI) ≥ 15/hr & ODI (3) ≥ 15).
- Diurnal (awake) BP≥135/85 or Nocturnal (sleep) BP≥120/70 mmHg based on 24hr Ambulatory Blood Pressure (24hr ABPM) determined at screening.

Exclusion Criteria

- Pregnancy.
- Abnormal Renal Function or Chronic Kidney Disease indicated by
- any of raised Creatinine (>110umol/L), raised Potassium (>5.0 mmol/L), low eGFR (<60ml/ min/1.73m2)
- Severe hypertension (SBP≥180 and/ or DBP≥110).
- Drug resistant hypertension defined as taking >3 classes of BP medication.
- Normal Office BP (< 140/90 mmHg) whilst taking anti-hypertensive medication that does not include an ACEI or ARB.
- ACE Inhibitor intolerance (based on the opinion of participants and study physicians) indicated by the development of new cough or symptoms of hypotension (dizziness).
- Unwilling to undergo washout of ACE or ARB medication.
- Shift workers who rotate to night shift.
- Poorly controlled diabetes defined as Glycosolated Haemoglobin (HbA1c) >=8
- Unstable Angina / Heart Failure (NYHA Class III and IV)/Stroke.
- Recent (< 6 months) AMI or Revascularisation Procedure.
- Significant Arrhythmia or Atrial Fibrillation.
- Cognitive impairment / Psychiatric disorder / Physically unable to participate.
- Recent OSA treatment with Mandibular Advancement Splint or
- CPAP exposure (within 3 months of screening) or prior refusal of
- CPAP treatment.
- Severe OSA (minimum oxygen saturation < 65% or RDI > 80) and excessively sleepy patients at increased risk for driving-related accidents requiring immediate treatment.
- More than 20% of AHI with central apnoeas.

Contact:

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OTHER

HEADACHE IN SLEEP DISORDERS – Dr Paul Hamor, Dr Keith Wong, Prof David Barnes, A/Prof Brendon Yee (DEPARTMENT OF RESPIRATORY MEDICINE, ROYAL PRINCE ALFRED HOSPITAL)

Summary
An increased prevalence of headaches is seen in patients with sleep disorders. This study aims to investigate whether there are any associations between those parameters measured during a sleep study and patients who suffer with headaches.

Recruitment target: 300

Design: Questionnaire

Inclusion Criteria
All patients undergoing a diagnostic sleep study at the Royal Prince Alfred Hospital or the Woolcock Institute of Medical Research will be invited to participate.

Exclusion criteria: inability to complete a questionnaire, e.g., language difficulties.

Study Procedure
Patients will receive an information sheet regarding the study and will have the opportunity to ask the sleep technician any questions they may have.

Patients who agree to participate will sign the consent form.

Patients who consent will be given 2 questionnaires, one to be completed just prior to their sleep study, and one in the morning at the completion of their sleep study.

The questionnaires will be collected by the sleep technician and kept with the patient's medical record until they are collected by the investigator.

Sleep studies will be scored independently and scorers will be blinded to the results of the headache questionnaire.

Data from sleep studies and questionnaires will be entered into a database by the investigator or his assistants, for analysis.

Contact:
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DEVELOPMENT OF AN OPTIMISED MULTIDISCIPLINARY INTERVENTION FOR POST-CANCER FATIGUE – PI Prof Sharon Naismith

Collaboration with UNSW, LifeStyle Clinic, BMRI. Earlier diagnosis and improved therapies have resulted in a markedly increased number of people successfully treated for cancer. It is estimated that there are 22 million cancer survivors worldwide, and 300,000 in Australia. Despite the fact that these individuals are cured of their cancer, many survivors face prolonged physical, emotional and social consequences resulting from their illness and its treatment. Prolonged fatigue is one of the most common and distressing symptoms reported by patients with cancer both during, and after, completion of treatment. As such cancer-related fatigue has substantive impacts on quality of life, it is a major focus of survivorship research.

The hypothesis underling this proposal is that a CBT program based on interventions for disturbances in activity patterns, sleep-wake cycle, and mood will significantly reduce symptom severity, and improve quality of life as well as functional status in patients with PCF. Furthermore, it is proposed that this program can be implemented widely via the application of a training and operations manual.

The overall aim of the project is therefore to establish an effective and reproducible CBT intervention for PCF, which can be implemented nationally and then internationally.

The specific aims are:

- To optimise assessment tools and intervention strategies for three CBT modules targeting disturbances in exercise/activity patterns, sleep-wake cycle, and mood in patients with PCF.
- To conduct a randomised controlled trial of optimised CBT versus a simple education program for patients with PCF.
- To develop a training package and an operations manual for the CBT program for PCF.

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